



REPLACEMENT SHEET
Title: CLONING, OVEREXPRESSION AND
THERAPEUTIC USE...
Appl. No.: 09/833,745
Inventors: Joseph ROBERTS *et al.*
Atty. Docket No. 078728-0106

Figure 1: Restriction pattern of the HAL coding region cut with selected enzymes.

HAL



N - NdeI site introduced at the N-terminus

B - BamHI site introduced at the C-terminus

E - EagI

P - PstI

S - SphI

Figure 2: Experimentally derived peptide sequences of HAL

N-terminal

(M)ASAPQITLGLSGATAD

Internal

(M)ALADLDELLDEA

(M)GEPVEREVLRA

Figure 3: SphI digestion pattern of HAL gene showing oligonucleotide and subclones.

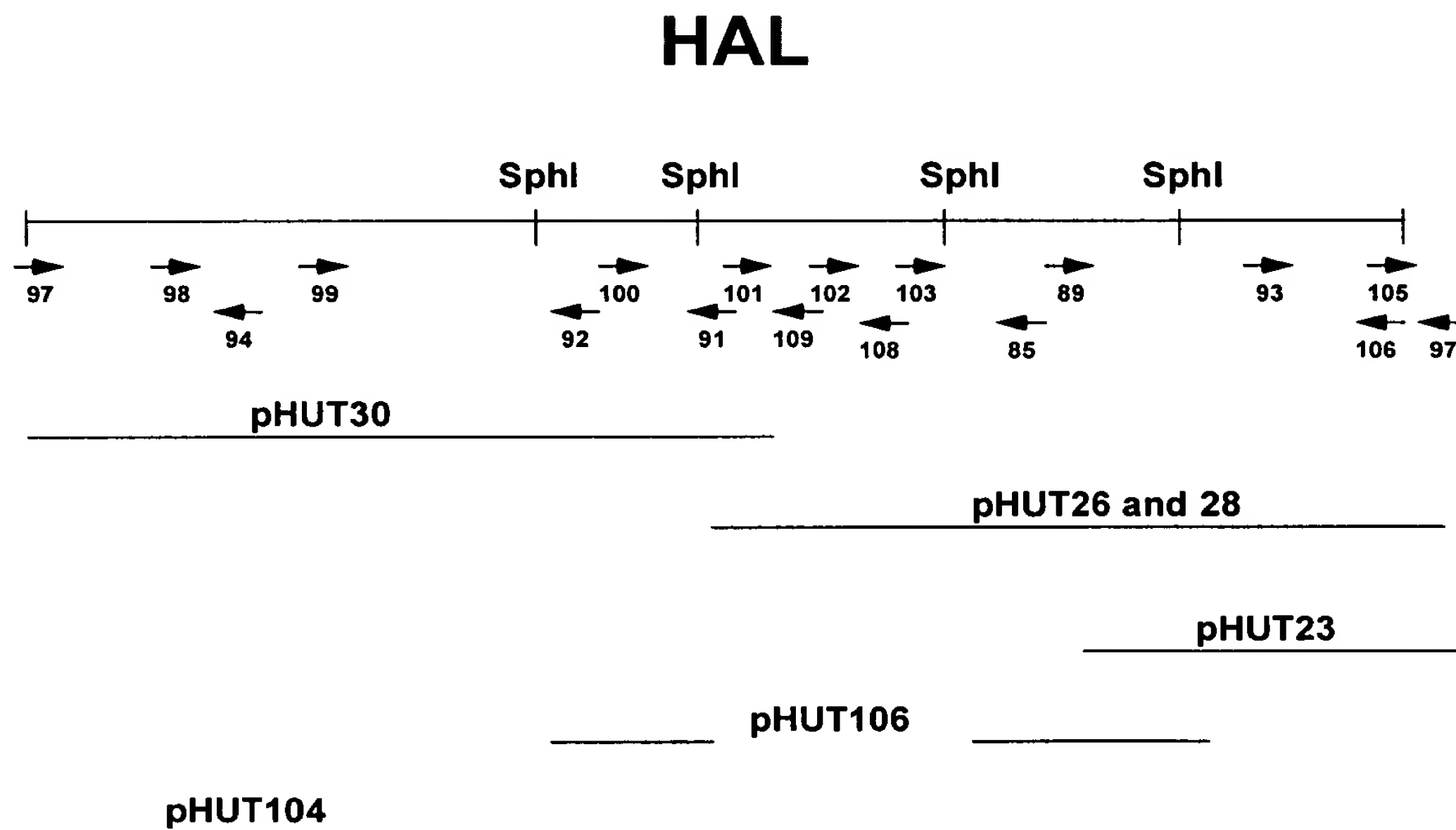
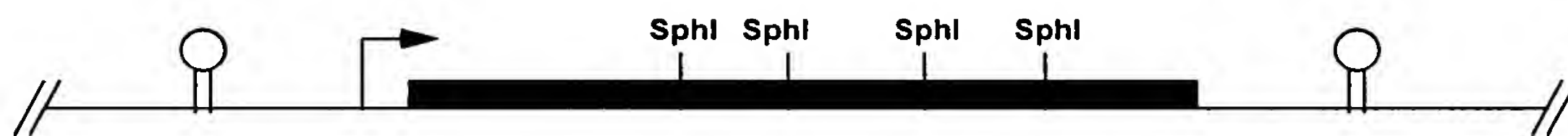


Figure 4: Histidine ammonia lyase overexpressing plasmid.

pHUT102



 ADI coding region

 T7 Promoter

 Transcriptional Terminator

Figure 5: SDS-PAGE showing expression of HAL in *E. coli*.

Lanes: 1 2 3 4



Figure 6: SDS-PAGE showing purification of HAL from *E. coli*

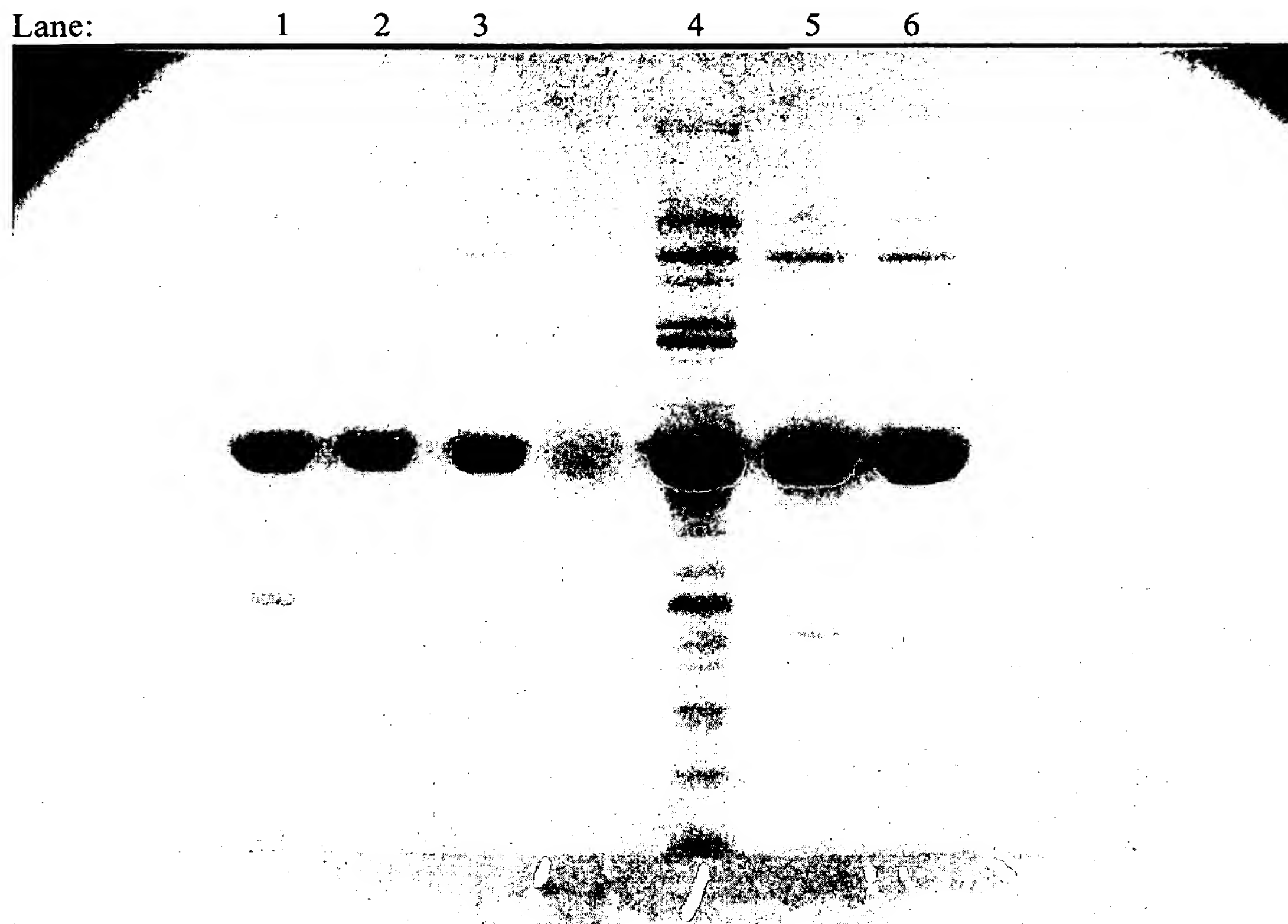


Figure 7: Effect of Temperature on HAL

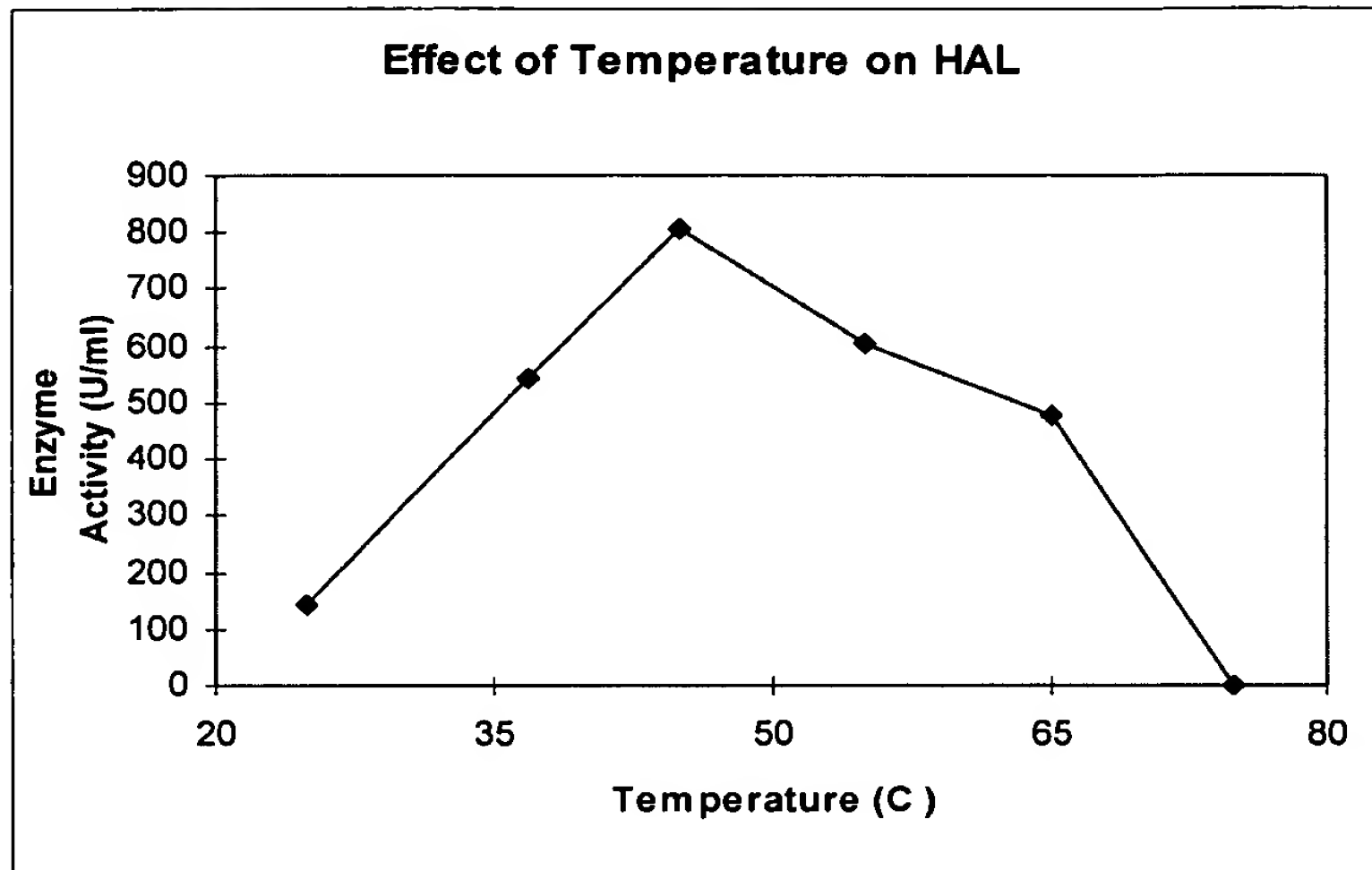


Figure 8: Effect of pH on HAL.

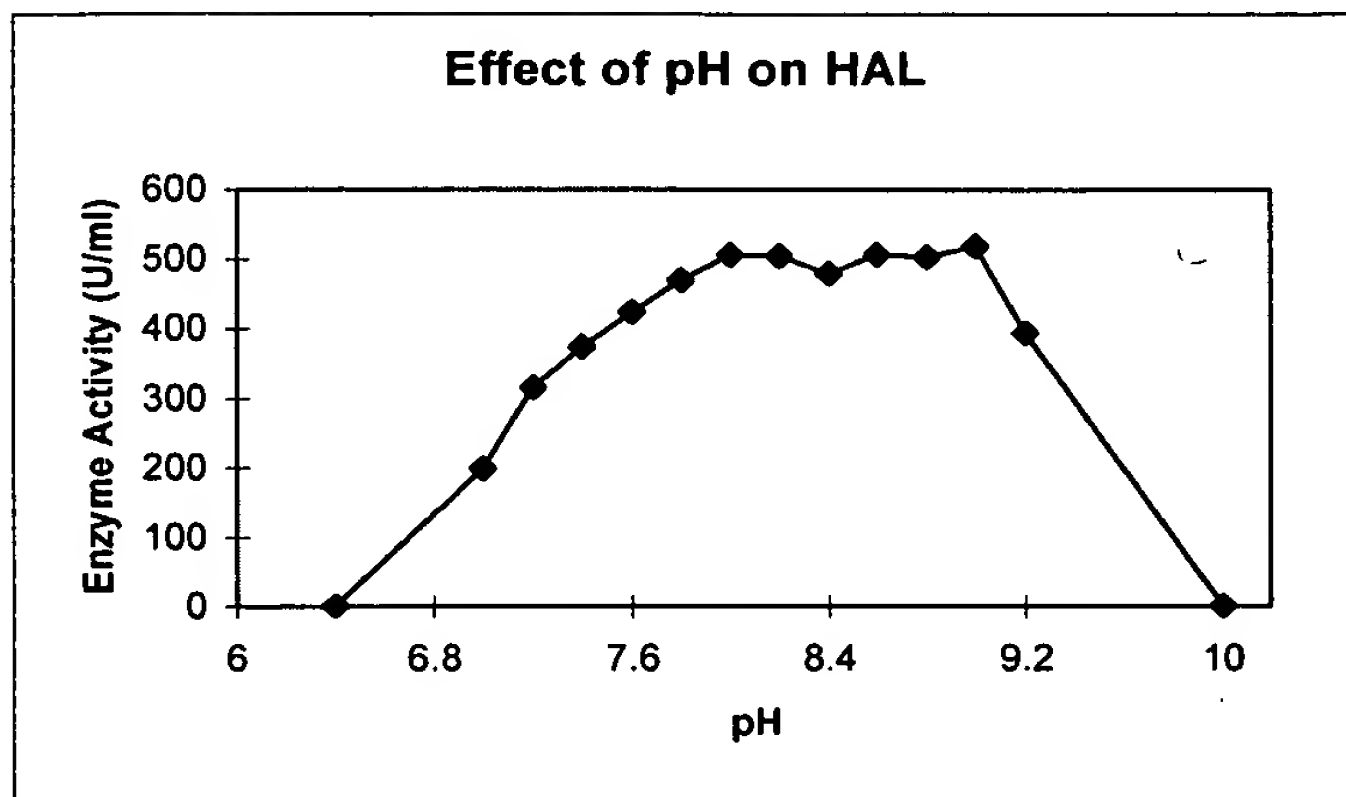


Figure 9: Effect of HAL and Histidinol on HSV.

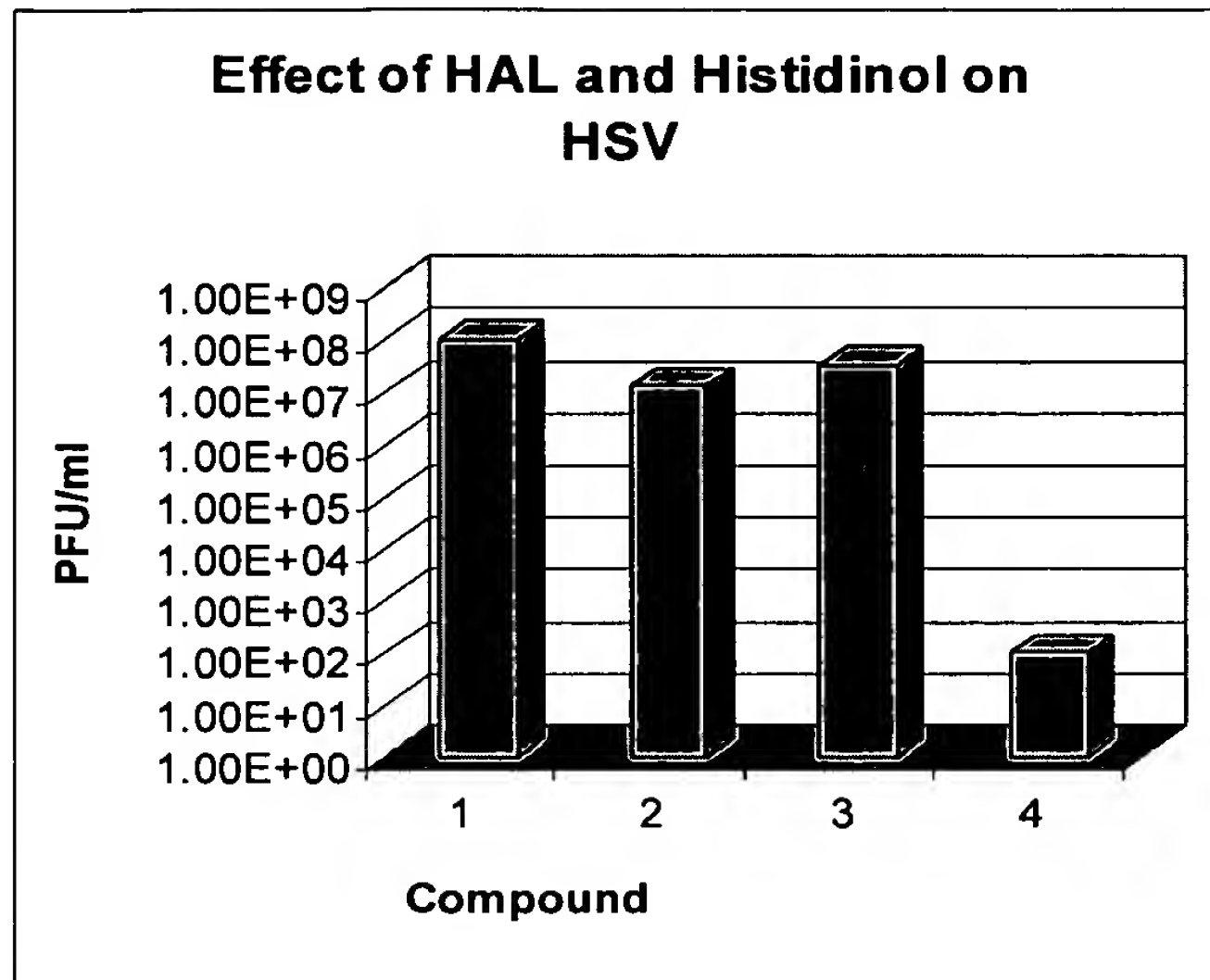


Figure 10: Effectiveness of L-histidinol as a Single Agent

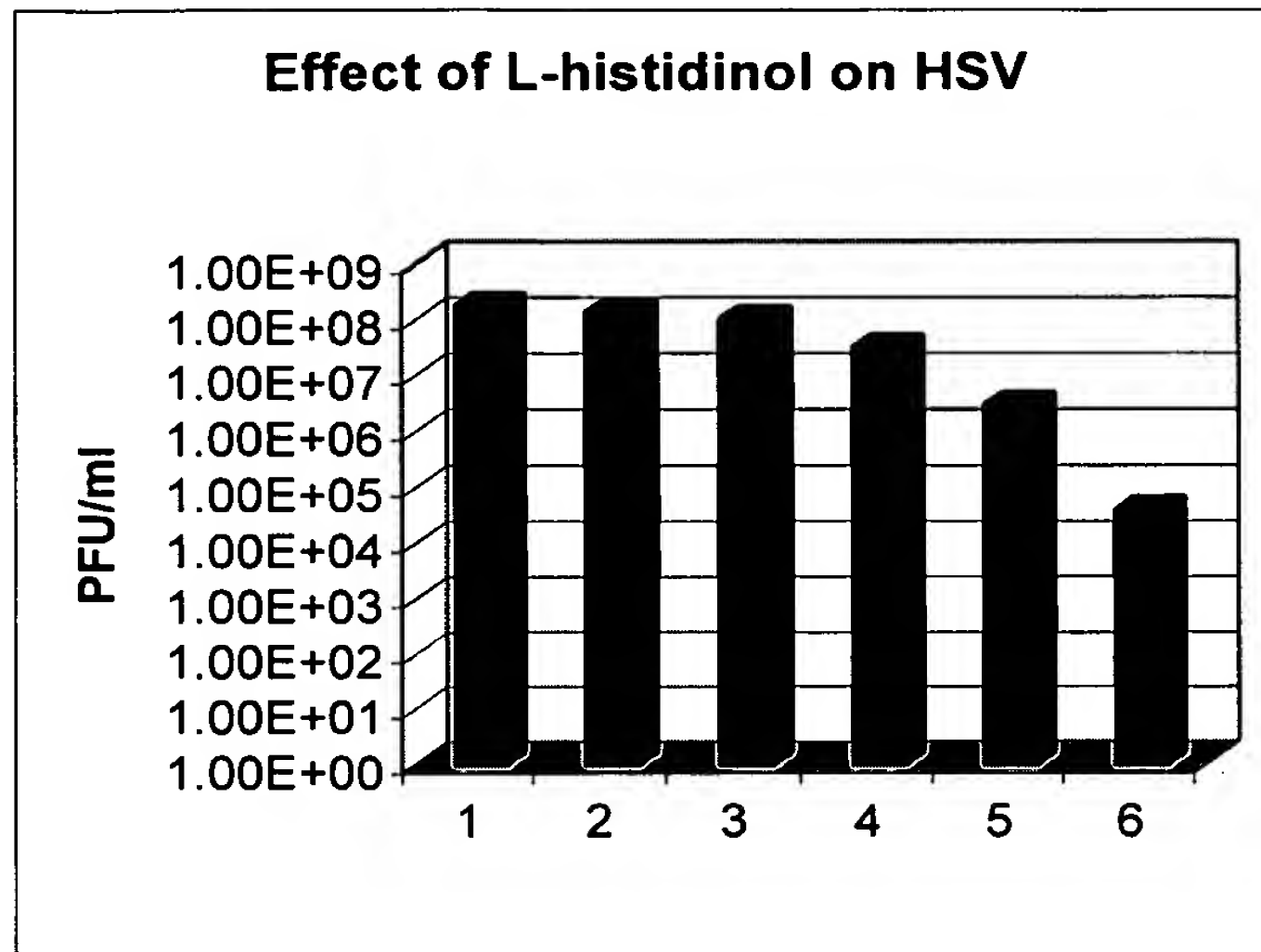


Figure 11: Effect of HAL and Histidinol on RSV.

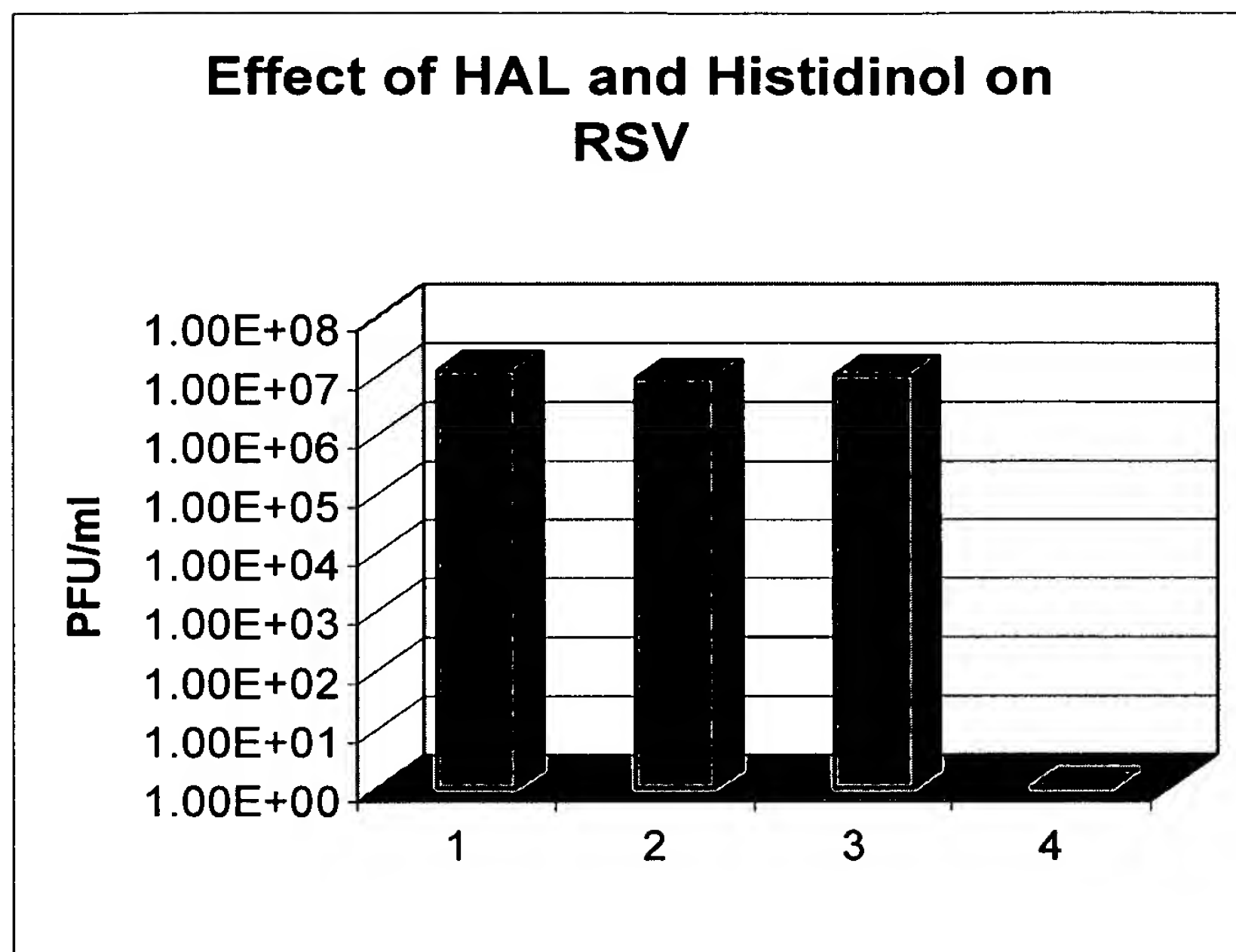


Figure 12: Effect of HAL on RMuLV.

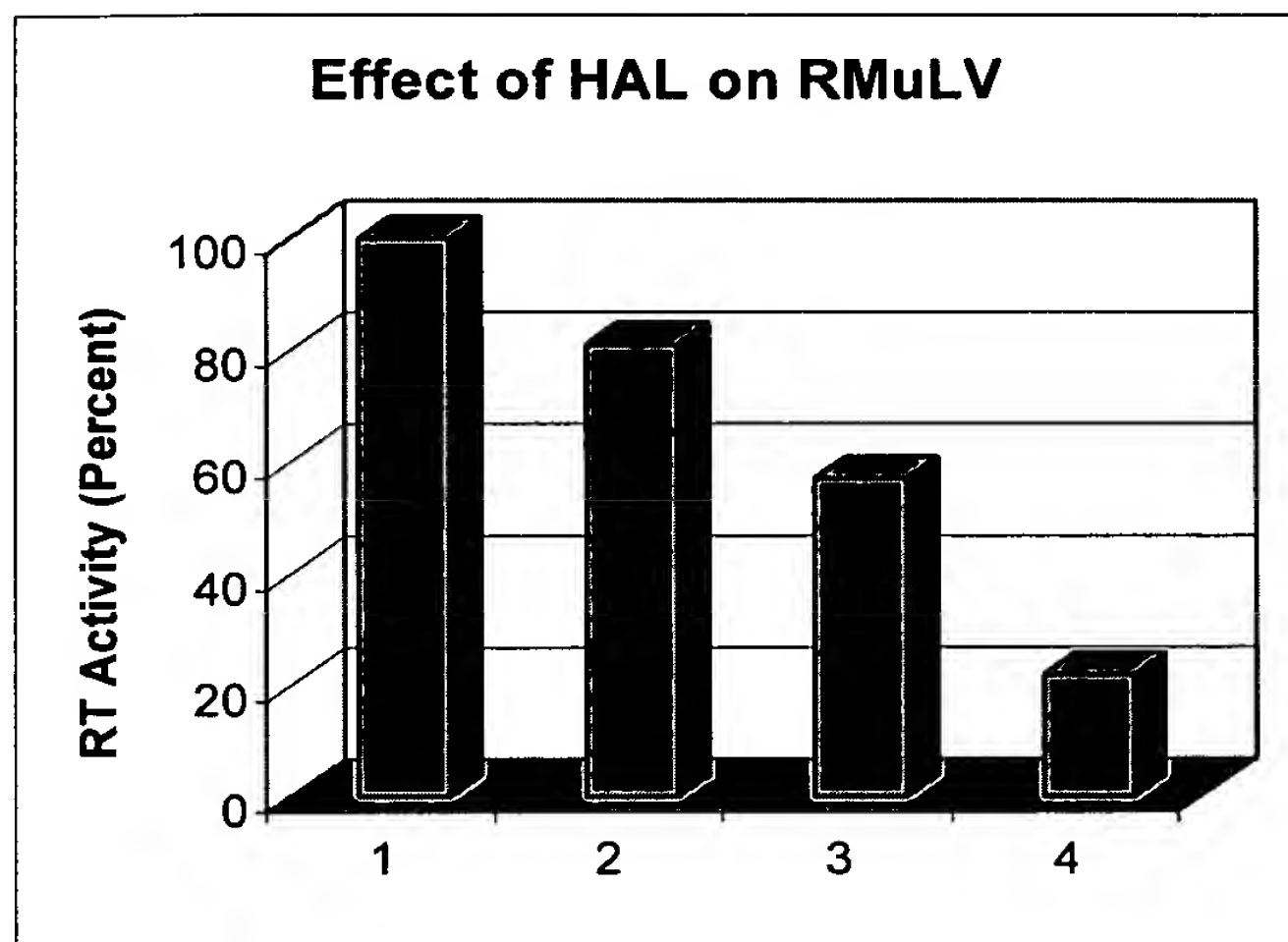


Figure 13A

```
HUTH_PSEPU -----
-
HUTH_RHIME -----
-
HUTH_MOUSE
MPRYTVHVRGEWLAVPCQDGKLTVGWLGREAVRRYMKNKPDNGGFTSVDEVQFLVHRCKG
HUTH_RAT
MPRYTVHVRGEWLAVPCQDGKLSVGWLGREAVRRYMKNKPDNGGFTSVDEVRFVRRCKG
HUTH_HUMAN
MPRYTVHVRGEWLAVPCQDAQLTVGWLGREAVRRYIKNKPDNGGFTSVDDAHFLVRRCKG
HUTH_CAEEL      -MRLQVQIGTECVVVPCKP-DDTIHAVAKKSVEKLRRLRPK-----
LPLADDYFEVRRTVG
HUTH_BACS -----
-
HUTH_STRGR -----
-
HUTH_CORY -----
-

HUTH_PSEPU -----
-
HUTH_RHIME -----
-
HUTH_MOUSE      LGLLDNEDELEVALEDNEFVEVVIEGDVMS-----PDFIPSQPEGVFLYSKYR---
-
HUTH_RAT        LGLLDNEDLLEVALEDNEFVEVVIEGDVMS-----PDFIPSQPEGVFLYSKYR---
-
HUTH_HUMAN      LGLLDNEDRLEVALENNEFVEVVIEGDAMS-----PDFIPSQPEGVYLYSKYR---
-
HUTH_CAEEL
NSLLDPEDLVSDVLKDSDFIIVAASVEETEDAKEAKKQEEIDNARAEIEKIDNRRRKVSF
HUTH_BACS -----
-
HUTH_STRGR -----
-
HUTH_CORY -----
-

HUTH_PSEPU -----
TELTLKPGTLTLAQLRAIHAAPVRLQLDASAAPIDASVACVEQIIA
HUTH_RHIME -----
MTVILRPGSVPLSDLETIYWTGAPARLDAAFDAGIAKAAARIAEIVA
HUTH_MOUSE -----
EPEKYIALDGDSLSTEDLVNLGKGGRYKIKLTSIAEKKVQQSREVIDSIIK
HUTH_RAT -----
EPEKYIALDGDSLSTEDLVNLGKGGRYKIKLTSIAEKKVQQSREVIDSIIK
HUTH_HUMAN -----
EPEKYIELDGDRLTTEDLVNLGKGGRYKIKLTPAEKRVQKSREVIDSIIK
HUTH_CAEEL
ADSLAPMVLAPPTKLLILDGNSLLPEDLVRCEKGECAIQLSMESEDRIKARTFLEKIAS
HUTH_BACS -----
MVTLDGSSLTTADVARVLFDFEEAAASEESMERVKKSRAAVERIVR
HUTH_STRGR -----
MDMHTVVVGTS GTTAEDVVAVARHGARVELSAAAVEALAAARLIVDALAA
HUTH_CORY -----
MASAPQITLGLSGATADDVIAVARHEARISISPVLEELASVRAHIDALAS
```

Figure 13B

HUTH_PSEPU
EDRTAYGINTGFGLLASTRIASHDLENLQRSVLVLSHAAGIGAPLDDDLVRLIMVLKINSL
HUTH_RHIME
GNAPVYGINTGFGKLASIKIDSSDVATLQARNLILSHCCGVGQPLTEDIVRLIMALKLISL
HUTH_MOUSE
ERTVVYGITTGFGKFARTVIPANKLQELQVNLVRSHSSGVGKPLSPERCRMLLALRINVL
HUTH_RAT
ERTVVYGITTGFGKFARTVIPANKLQELQVNLVRSHSSGVGKPLSPERCRMLLALRINVL
HUTH_HUMAN
EKTVVYGITTGFGKFARTVIPINKLQELQVNLVRSHSSGVGKPLSPERCRMLLALRINVL
HUTH_CAEEL
EHRAVYGVTTGFGTFSNVTIPPEKLKKLQNLIRSHATGYGEPLAPNRARMMLLALRINIL
HUTH_BACS
DEKTIYGINTGFGKFSDVLIQKEDSAALQNLILSHACGVGDPFPECVSRAMLLLRANAL
HUTH_STRGR
KPEPVYGVSTGFGALASRHIGTELRAQLQARNIVRSHAAGMGPRVEREVVRALMFLRLKTV
HUTH_CORY
ADTPVYGISTGFGALATRHIAPEDRAKLQRSILIRSHAAGMGEPVEREVVRALMFLRAKTL

HUTH_PSEPU
SRGFSGIRRKVIDALIALVNAEVYPHIPLKGSVGASGDLAPLATMSLVLLGEGKARYKGQ
HUTH_RHIME
GRGASGVRLELVRLIEAMLDKGVIPLIPEKGSVGASGDLAPLAHMAAVMMGHGEAFFAGE
HUTH_MOUSE
AKGYSGISLETLKQVIEAFNASCLSYVPEKGTVGASGDLAPLSHLALGLIGEGKMWSPKS
HUTH_RAT
AKGYSGISLETLKQVIEVFNASCLSYVPEKGTVGASGDLAPLSHLALGLIGEGKMWSPKS
HUTH_HUMAN
AKGYSGISLETLKQVIEMFNASCLPYVPEKGTVGASGDLAPLSHLALGLVGEKGMWSPKS
HUTH_CAEEL
AKGHSGISVENIKMIAAFNAFCVSYVPQQGTVGCSGDLCPALHLALGLLGEGKMWSPTT
HUTH_BACS
LKGFSGVRAELIEQLLAFLNKRVPVIPPQQSLGASGDLAPLSHLALALIGQGEVFFEGE
HUTH_STRGR
ASGHTGVRPEVAQTMADVNLNAGITPVVHEYGSLGCSGDLAPLSHCALTLMGEGEAEGPDG
HUTH_CORY ASGRS-
VRPVVLETMVGMLNAGITPVVREYGSLGCSGDLAPLSHCALVLMGEGEATDAHG

HUTH_PSEPU -
WLSATEALAVAGLEPLTLAAKEGLALLNGTQASTAYALRGLFYAEDLYAAAIACGGLSV
HUTH_RHIME -
RMKGDAALKAAGLSPVTLAAKEGLALINGTQVSTALALAGLFRAHRAGQAALITGALST
HUTH_MOUSE
GWADAKYVLEAHGLKPIVLKPKEGLALINGTQMITS LGCEALERASAIARQADIVAALTL
HUTH_RAT
GWADAKYVLEAHGLKPIVLKPKEGLALINGTQMITS LGCEAVERASAIARQADIVAALTL
HUTH_HUMAN
GWADAKYVLEAHGLKPVILKPKEGLALINGTQMITS LGCEAVERASAIARQADIVAALTL
HUTH_CAEEL
GWQPADVVLKKNLEPLELGPKEGLALINGTQMVTALGAYTLERAHNIARQADVIAALSL
HUTH_BACS -
RMPAMTGLKKAGIQPVTLSKEGLALINGTQAMTAMGVVAYIEAEKLAYQTERIASLTI
HUTH_STRGR
TVRPAGELLAHGIAPVELREKEGLALLNGTDGMLGMLVMALADLRNLYTSADITAALSL
HUTH_CORY
DIRPVPELFAEAGLTPVELAEKEGLALVNGTDGMLGQLIMALADLDELLDIADATAAMSV

Figure 13C

HUTH_PSEPU EAVLGSRSPFDARIHE-ARGQRGQIDTAACFRDLLGDSSEVSLSHKNCD-----
KVQDPYS
HUTH_RHIME DAAMGSSAPFHPDIQH-CAAIRARSTRAAALRQLLTG-SPIRQSHIEGDE---
RVQDPYC
HUTH_MOUSE EVLKGTTKAFDTDIHA-VRPHRGQIEVAFRFRSL LDS-
DHHPSEIAESHRFCDRVQDAYT
HUTH_RAT EVLKGTTKAFDTDIHA-VRPHRGQIEVAFRFRSL LDS-
DHHPSEIAESHRFCDRVQDAYT
HUTH_HUMAN EVLKGTTKAFDTDIHA-LRPHRGQIEVAFRFRSL LDS-
DHHPSEIAESHRFCDRVQDAYT
HUTH_CAEL DVLKGTTRAYDPDIHR-IRPHRGQNLSALRLRALLHS-
EANPSQIAESHRNCTKVQDAYT
HUTH_BACS EGLQGIIDAFDEDIHL-ARGYQEQIDVAERIRFYLS-GLTTSQGE-----
LRVQDAYS
HUTH_STRGR EALLGTDKVLAPELHA-IRPHPGQGVSA DNMSRVLAG-SGLTGHHQDDAP---
RVQDAYS
HUTH_CORY EAQLGTDQVFRAELHEPLRPHPGQGRSAQNMFAFLAD-SPIVASHREGDG---
RVQDAYS

HUTH_PSEPU
LRCQPQVMGACLTQLRQAAEVLGIEANAVSDNPLVFAAEGDVISGGNFHAEFPVAMAADNL
HUTH_RHIME IRCQPQVDGACLDLLRSVAATLTIEANAVTDNPLVLSDN-
SVVSGGNFHAEPVAFADQI
HUTH_MOUSE
LRCCPQVHG VVNDTIAFVKDIITTELNSATDNPMVFASRGETISGGNFHGEYPAKALDYL
HUTH_RAT
LRCCPQVHG VVNDTIAFVKDIITTELNSATDNPMVFASRGETISGGNFHGEYPAKALDYL
HUTH_HUMAN
LRCCPQVHG VVNDTIAFVKNIITTELNSATDNPMVFANRGETVSGGNFHGEYPAKALDYL
HUTH_CAEL
LRCVPQVHG VVHDTIEFVREIITTEMNSATDNPLVFADREEIISGGNFHGEYPAKALDFL
HUTH_BACS
LRCIPQVHGATWQTLGYVKEKLEIEMNAATDNPLIFNDGDKVISGGNFHGOPIAFAMDFL
HUTH_STRGR VRCAPQVNGAGRDTLDHAALVAGRELASSVDNPVVLPG-
RVESNGNFHGAPVAYVLDL
HUTH_CORY LRCSPQVTGAARDTIAHARLVATRELAAIDNPVVLPSG-
EVTSNGNFHGAPVAYVLDL

HUTH_PSEPU ALAI AEIGSLSERRISLMMDKHMS-
QLPPFLVENGGVNSGFMIAQVTAAALASENKALSH
HUTH_RHIME
ALAVCEIGAISQRRIALLVDPALSLRLPAFLAKKPGLNSGLMIAEVTSAALMSENKQLSH
HUTH_MOUSE AIGVHELAAISERRIERLCNPSLS-
ELPAFLVAEGGLNSGFMIAHCTAAALVSESKALCH
HUTH_RAT AIGVHELAAISERRIERLCNPSLS-
ELPAFLVAEGGLNSGFMIAHCTAAALVSESKALCH
HUTH_HUMAN AIGIHELAAISERRIERLCNPSLS-
ELPAFLVAEGGLNSGFMIAHCTAAALVSENKALCH
HUTH_CAEL AIAVAELAQMSERRLERLVNKELS-
GLPTFLTDPDGLNSGFMTVQLCAASLVSENKVLCH
HUTH_BACS KIAISELANIAERRIERLVNPQLN-
DLPPFLSPHPGLQSGAMIMQYAAASLVSENKTLAH
HUTH_STRGR
AIVAADLGSICERRTRDLLDKNRSHGLPPFLADDAGVDSGLMIAQYTQAALVSEMKRLAV
HUTH_CORY
AIAVADLGSIAERRTRMLDPAARSRLPAFLADDPGVDSGMMIAQYTQAGLVAENKRLAV

Figure 13D

HUTH_PSEPU	PHSVDSLPTSANQEDHVSMAPAAGKRLWEMAENTRGVPAIEWLGACQGLDLRKG-LKTS
HUTH_RHIME	PASVDSTPTSANQEDHVSMACHGARRLLQMTENLFSIIGIEALAAVQGIEFRAP-LTTS
HUTH_MOUSE	PSSVDSLSTSAATEDHVSMGGWAARKALRVVEHVEQVLAIELLAACQGIEFLRP-LKTT
HUTH_RAT	PSSVDSLSTSAATEDHVSMGGWAARKALRVIEHVEQVLAIELLAACQGIEFLRP-LKTT
HUTH_HUMAN	PSSVDSLSTSAATEDHVSMGGWAARKALRVIEHVEQVLAIELLAACQGIEFLRP-LKTT
HUTH_CAEEL	PSSVDSIPTSCNQEDHVSMGGFAARKALTVVEHVEAVLAMELLAACQGIEFLKP-LIST
HUTH_BACS	PASVDSIPSSANQEDHVSMGTIAARHAYQVIANTRRVIAIEAICALQAVEYRGI-EHAA
HUTH_STRGR	
PASADSI PSSAMQEDHVSMGWSAARKLRTAVDNLARIVAVELYAATRAIELRAAEGLT PA	
HUTH_CORY	PA-VDSIPSSAMQEDHVSLGWHAARKLPTSVANLRRILAVEMLIAGRALDLRAP-LKPG
HUTH_PSEPU	AKLEKARQALRSEVA-HYDRDRFFAPDIEKAVELLAKG---S-LTGLLPAGVLP SL---
-	
HUTH_RHIME	PELQKAAA AVRGVSS-SIEEDRYMADDLKAAGDLVASG---R-LAAAVSAGILPKLEN-
HUTH_MOUSE	TPLEKVYDLVRSVVR-
PWIKDRFMAPDIEAAHRLLLDQKVWEVAAPYIEKYRMEHIPESR	
HUTH_RAT	TPLEKVYDLVRSVVR-
PWIKDRFMAPDIEAAHRLLLDQKVWEVAAPYIEKYRMEHIPESR	
HUTH_HUMAN	TPLEKVYDLVRSVVR-
PWIKDRFMAPDIEAAHRLLEQKVWEVAAPYIEKYRMEHIPESR	
HUTH_CAEEL	APLHKIYQLVRSVAP-
PLNEDRYMKPEIDAVLEMIRENRIWEAVLPHLETLEAMEELDPD	
HUTH_BACS	SYTKQLFQEMRKVVP-SIQQDRVFSYDIERLTDWLKK---ESLIPDHQNKELRGMNI-
HUTH_STRGR	PASEAVVAALRAAGAEGPGPDRFLAPDLAAADTFVREG---R-LVAAVEPVTGPLA---
-	
HUTH_CORY	PATGAVLEVLR SKVA-GPGQDRFLSAELEAAYDLLANG---S-VHKALEAHLPE-----
-	
HUTH_PSEPU	-----
HUTH_RHIME	-----
HUTH_MOUSE	PLSPTAFSLES LRKNSATIPESDDL----
HUTH_RAT	PLSPTAFSLES LRKNSATIPESDDL----
HUTH_HUMAN	PLSPTAFSLQFLHKKSTKIPESEDL----
HUTH_CAEEL	ALRQFTKTPTGIVQDRSMIPISDDEESIE
HUTH_BACS	-----
HUTH_STRGR	-----
HUTH_CORY	-----

Figure 14A

983831	100.0%	[. MASAPQITLGLSGATADDVIAVARHEARISISIPQVLEELASVRAHIDALASADTPVYIGISTGFGALATRHIAPIEDRAKLQ
1 SWALL: CAC21618	66.1%	---	MHTVVGTSGVTASDVAVARAGARIELSEEAVALAAARSVVDALAAKPDVPYGVSTGFGALATRHISPELRGRLO
2 SWALL: HUTH_STRGR	65.4%	-	MDMHTVVGTSGTTAEDVVAVARHGARVELSAAAVEALAAARLIVDALAAKPEVPYGVSTGFGALASRHIGTELRAQLQ
3 SWALL: HUTH_DEIRA	46.8%	----	MILDRDLNLEQFISVVRHGEQVELSAAARERIRARARTVIEQIVEGDTPYGVNTGFGKFENVQIDRSQLAQLQ
4 SWALL: BAB16159	42.0%	-----	VPLHLADIYWNNGSAKLDPSFDAAVLKGAAARIAEIAAGNAPVYGINTEGFGKLASIKIDAADLTLQ
5 SWALL: Q9KWE4	42.0%	-----	VPLHLADIYWNNGSAKLDPSFDAAVLKGAAARIAEIAAGNAPVYGINTEGFGKLASIKIDAADLTLQ
6 SWALL: HUTH_BACSU	40.4%	-----	MVTLDGSSLTADVARVLFDEEAAAASEESMERVKKSRAAVERIVRDEKTIYGINTEGFGKFSVDVLIQKEDSAAALQ
7 SWALL: Q9KSQ4	42.2%	--	MLHLMIKPGQLSLKOLRQVSRSPVLSLDPEAIPAIAESAQVVEQVISEGRTVYGINTEGFGLLANTKIAPODLETLQ
8 SWALL: Q9HU85	41.7%	----	MSLHLKPGQLTLADLRQAYLAPVRLSLDPSADAPIAASVACVENIIAEGRTAYGINTEGFGLLASTRISPADLEKLQ
9 SWALL: Q9KBE6	39.3%	--	MTNLKLLDGRSLSLHDLHRIIYEGETVGASDESMKEVKQSRKAVEQIVADEKIIYGITTGFGKFSDFIDPDDVLENLQ
10 SWALL: HUTH_PSEPU	41.7%	----	TELTLPKPGTLTLAQLRAIHAAPVRLQLDASAAPDAIDASVACVEQIIAEDRTAYGINTEGFGLLASTRIASHDLENLQ
11 SWALL: HUTH_RHIME	40.6%	-----	LRPGSVPLSDLETIYWTGAPARLDAADFAGIAKAAARIAEIVAGNAPVYGINTEGFGKLASIKIDSSDVATLQ
12 SWALL: Q9HU90	40.7%	MSDL	PSVFGDPLRWQELVAVARHGARLELSAAAWARIDNARAIVCRIVANGERAYGISTGLGALCDVLLEGEQLAELS
13 SWALL: HUTH_HUMAN	39.2%	KYRE	PEKYIELDGLTTEDLVNLKGGRYKIKLPTAEKRVQKSREVIDSIIKEKTVVYGITTGFGKFA-RTVIPINKLQLO
14 SWALL: HUTH_CAEEL	38.8%	VLAP	PTKLLILDGNSPEDLVRCEKGECAIQLSMESEDRIKARTFLEKIASEHRAVYGVTTGFGTFSNVTIPPEKCLKLO
15 SWALL: Q9HLI6	41.0%	----	MIEIDGRSLRVEDVYAVAVEYDRVSIISDRTLKAVEEKHEAFLKLINSKGTVYGVNTGFGSLNVHIERDQEIELQ
16 SWALL: HUTH_MOUSE	38.6%	KYRE	PEKYIALDGDSTEDLVNLKGGRYKIKLTSIAEKKVQQSREVIDSIIKERTVVYGITTGFGKFA-RTVIPANKLQLO
17 SWALL: BAB29407	38.6%	KYRE	PEKYIALDGDSTEDLVNLKGGRYKIKLTSIAEKKVQQSREVIDSIIKERTVVYGITTGFGKFA-RTVIPANKLQLO
18 SWALL: HUTH_RAT	38.2%	KYRE	PEKYIALDGDSTEDLVNLKGGRYKIKLTSIAEKKVQQSREVIDSIIKERTVVYGITTGFGKFA-RTVIPANKLQLO
19 SWALL: AAG53586	39.8%	----	MNALTLPGTTLTLAQLRVWQQPLQTLDESAHEAINDSVACVEAIVAEGRAYGINTEGFGLLAQTRIATHDLENLQ
20 SWALL: Q9KKE0	38.9%	----	MGEMISLDGPLTWREIASIAEGASLDLSGPARLRIAQARRIVDALVERGIRGYGINTEGFGALCDVIIISRENQOALS
21 SWALL: Q9HQD5	42.2%	-----	MSDTRIDAADREALQ

Figure 14B

	81	1	:	160				
983831	100.0%	RSLIRSHAAGMGE	PVEREVVRALMFLRAKTLASGR	TGVRPVVLETMVGMNLNAGITPVVREYSGSLGCSGDLAPLSHCALVL				
1 SWALL: CAC21618	66.1%	RNIVRSHAAGMGP	VEREVVRALMFLRLKTVCSGR	TGVRPEVAQTMADVNLNAGITPVVHEYSGSLGCSGDLAPLSHCALT				
2 SWALL: HUTH_STRGR	65.4%	RNIVRSHAAGMGP	VEREVVRALMFLRLKTVASGHT	GTGVRPEVAQTMADVNLNAGITPVVHEYSGSLGCSGDLAPLSHCALT				
3 SWALL: HUTH_DEIRA	46.8%	HNLIIVSHAIGMGE	PLPAEVVRGMLLRAQSLSLGH	SGVRVEVELLLALLNADALPVVPSQSGSVGASGDLAPLAHLAIGL				
4 SWALL: BAB16159	42.0%	RNLIILSHCCGVGA	PLPENNVRLIMALKLISLGR	GASGVRIELIRLIEGMLEKGVIPVIPEKGSVGASGDLAPLAHMSATM				
5 SWALL: Q9KWE4	42.0%	RNLIILSHCCGVGA	PLPENNVRLIMALKLISLGR	GASGVRIELIRLIEGMLEKGVIPVIPEKGSVGASGDLAPLAHMSATM				
6 SWALL: HUTH_BACSU	40.4%	LNLIILSHACGVGD	PFPECVSRAMLLLRANALLK	GFSGVRAELIEQLLAFLNKR	VHPVIPPQQGSLGASGDLAPLSHLALAL			
7 SWALL: Q9KSQ4	42.2%	KSIVLSHAAGIGE	LMSTVRLMMLLKINSLARG	YSGIRLEVIQALIELVNNQI	YPCVPKKGSVGASGDLAPLAHMSTVL			
8 SWALL: Q9HU85	41.7%	RSIVLSHAAGVGE	ALDDAMVRLVMLLKVN	SLARGFSGIRRKVIDALIALINAE	VYPHIPPLKGSVGASGDLAPLAHMSLVL			
9 SWALL: Q9KBE6	39.3%	HNLIYSHACGVGS	PPFETVSRMTLVLRANALLK	GFSGVRPLVIERLLALVNANI	HPVIPPQQGSLGASGDLAPLSHLALVL			
10 SWALL: HUTH_PSEPU	41.7%	RSLVLSHAAGIGA	PLDDDLVRLIMVLKINSL	SRGFSGIRRKVIDALIALVNAE	VYPHIPPLKGSVGASGDLAPLAHMSLVL			
11 SWALL: HUTH_RHIME	40.6%	RNLIILSHCCGVQ	PLTEIVRLIMALKLISLGR	GASGVRLVRLIEAML	DKGVIPLIPEKGSVGASGDLAPLAHMAAVM			
12 SWALL: Q9HU90	40.7%	RNTLLSHACGVGE	PLRDEQTRAIICAAVANYS	QKSGLDRLSVEGLLALLNHG	ITPQVPAQGSVGY---LTHMAHV	GIAL		
13 SWALL: HUTH_HUMAN	39.2%	VNLVRS	SHSSGVGKPLSPER	CRMLLALRINVLAKGYS	GISLET	LKQVIE	MFNASCLPYVPEKGT	VGASGDLAPLSHLALGL
14 SWALL: HUTH_CAEEL	38.8%	LNLIIRSHATGY	GEPLAPNRARMLLALRINILAK	GHSGISVENIKKMI	AFNAFCVSVYPQ	QGT	VGC	SGDLCPLAHLALGL
15 SWALL: Q9HLI6	41.0%	KNLIIRSHSSGVGD	YLENRYVRAIMAVRLNSLAAGY	SAVSADLLNMMVEM	LNDRDVI	PAVPKY	GSVGASGDLAPLAHIGLAM	
16 SWALL: HUTH_MOUSE	38.6%	VNLVRS	SHSSGVGKPLSPER	CRMLLALRINVLAKGYS	GISLET	LKQVIE	AFNASCLSVVPEKGT	VGASGDLAPLSHLALGL
17 SWALL: BAB29407	38.6%	VNLVRS	SHSSGVGKPLSPER	CRMLLALRINVLAKGYS	GISLET	LKQVIE	AFNASCLSVVPEKGT	VGASGDLAPLSHLALGL
18 SWALL: HUTH_RAT	38.2%	VNLVRS	SHSSGVGKPLSPER	CRMLLALRINVLAKGYS	GISLET	LKQVIE	FNASCLSVVPEKGT	VGASGDLAPLSHLALGL
19 SWALL: AAG53586	39.8%	RSLVLSHAAGVGE	PLDDDIVRLMMVLKINSLARG	FSGIRLSVIOALIALVNAG	YSVDPAKGSVGASGDLAPLAHMSLTL			
20 SWALL: Q9KKE0	38.9%	RNIILSHACGVGD	PLGRVEARAVMAAQIANLTHG	YSGVRVETAEMLLALLNADI	IPLIPSRGSVGY-----LTHAA	LV		
21 SWALL: Q9HQD5	42.2%	ANLVRSHAAGAG	SELDTAAVRALLVTRLNALAKGYS	GIRERVDVLVGLLNEG	VHPVVPVPSRGS	SLGASGDLAPLAHMSRVL		

Figure 14C

	983831	161	2	240
1	SWALL: CAC21618	100.0%	MGEGEATDAHGDIRPVPELFAEAGLTPVELAEKEGLALVNGTDGMLGQLIMALADLDELDDIADATAAMSVEAQLGTDQV	
2	SWALL: HUTH_STRGR	66.1%	MGEEDAEGPDGTVRPAGELLAAHGIAPVELREKEGLALINGTDGMLGMLVMALADLDTLYKSADITAAALTMEALLGTDREV	
3	SWALL: HUTH_DEIRA	65.4%	MGEGEAEGPDGTVRPAGELLAAHGIAPVELREKEGLALINGTDGMLGMLVMALADLRLNLYTSADITAAALSLEALLGTDKV	
4	SWALL: BAB16159	46.8%	IGLGLDI-EYQGQVRPAADVLAELGLSPVQLQAKEGLALINGTQLMGSLALALHDAQVLLGTANLAAAMTVEARYGSHRP	
5	SWALL: Q9KWE4	42.0%	MGEGEAF-YQGVQMPSKDALAKAGLSPVVLAAKEGLALINGTQTSTALALAGLFRAHRAAQSAALVTGALSTDAAMGSSAP	
6	SWALL: HUTH_BACSU	42.0%	MGEGEAF-YQGVQMPSKDALAKAGLSPVVLAAKEGLALINGTQTSTALALAGLFRAHRAAQSAALVTGALSTDAAMGSSAP	
7	SWALL: Q9KSQ4	40.4%	IGQGEVF-FEGGERMPAMTGLKKAGIQPVTLTSTKEGLALINGTQAMTAMGVVAYIEAEKLAYQTERIASLTIEGLQGIIDA	
8	SWALL: Q9HU85	42.2%	LGEQQRAR-YNGKIIISGLEAMKIAGLEPITLAPKEGLALINGTQASTAFALGLEGLFVAEDLFASATVCGAMSVEAALGSRRP	
9	SWALL: Q9KBE6	41.7%	IGESRARH-RGEWLPAAEALAVAGLEPLTLAAKEGLALINGTQVSTAYALRGLFEAEDLFAAATVCGGLSVEAMLGSRAP	
10	SWALL: HUTH_PSEPU	39.3%	LGEGEVF-YKGTCTKASFALKEEIEIPITLTAKKEGLALINGTQAMTAMGVVAYIEAEKLAQFQSEIIASLTMEGLRGIIDA	
11	SWALL: HUTH_RHIME	41.7%	LGEQKAR-YKQWLSATEALAVAGLEPLTLAAKEGLALINGTQASTAYALRGLFYAEDLYAAAIACGGLSVEAALGSRSP	
12	SWALL: Q9HU90	40.6%	MGHGEAFFAGERMKGDAALKA-AGLSPVTLAAKEGLALINGTQVSTALALAGLFRAHRAQQAALITGALSTDAAMGSSAP	
13	SWALL: HUTH_HUMAN	40.7%	LGIGEVVS-YRGSVVPAALAAEGLATVRLGAKDGLCLVNGTPCMTGLACLALDDAQRLAQWADVIGAMSFEALRGQLAA	
14	SWALL: HUTH_CAEEL	39.2%	VGEKMWSPKSGWADAKYVLEAHGLKPVILKPKKEGLALINGTQMITSLGCEAVERASAIARQADIVAALTLLEVILKGTTKA	
15	SWALL: Q9HLI6	38.8%	LGEKMWSPPTGWQPADVVLKNNLEPLELGPKEGLALINGTQMVLTALGAYTLERAHNIARQADVIAALSVDLVKGTTRA	
16	SWALL: HUTH_MOUSE	41.0%	MGEKAF-FEGRMLDSARALEKAGLKPYPQFKEKEGVALINGTSFMSGILSIAVMDAHDILENAIRSALLSFEALGGTSKA	
17	SWALL: BAB29407	38.6%	IGEGKMWSPKSGWADAKYVLEAHGLKPIVLKPKKEGLALINGTQMITSLGCEALERASAIARQADIVAALTLLEVILKGTTKA	
18	SWALL: HUTH_RAT	38.6%	IGEGKMWSPKSGWADAKYVLEAHGLKPIVLKPKKEGLALINGTQMITSLGCEALERASAIARQADIVAALTLLEVILKGTTKA	
19	SWALL: AAG53586	38.2%	IGEGKMWSPKSGWADAKYVLEAHGLKPIVLKPKKEGLALINGTQMITSLGCEAVERASAIARQADIVAALTLLEVILKGTTKA	
20	SWALL: Q9KKE0	39.8%	LGEQKAR-YRGEWLPAAALQKAGLAPVTLAAKEGLALINGTQASTAFALRGLFEAEDLFASAVVCGALTTEAVLGSRRP	
21	SWALL: Q9HQD5	38.9%	IGHGSAMQGTTERLSGADAL-ARLGLAPLRLEAKEGLSLVNGTPCATGLAALALARTERLFAWADAAAAMTYE-NLGSQAN	
		42.2%	IGEGQA-DVAGERMPAAEALAAADLEPVTLQAKEGLALINGTQLTGTGVAALALVDAERVLRSDTAGALTTEVTMTSTAS	

Figure 14D

	983831	241	100.0%	:	3	320
1	SWALL: CAC21618		66.1%			
2	SWALL: HUTH_STRGR		65.4%			
3	SWALL: HUTH_DEIRA		46.8%			
4	SWALL: BAB16159		42.0%			
5	SWALL: Q9KWE4		42.0%			
6	SWALL: HUTH_BACSU		40.4%			
7	SWALL: Q9KSQ4		42.2%			
8	SWALL: Q9HU85		41.7%			
9	SWALL: Q9KBE6		39.3%			
10	SWALL: HUTH_PSEPU		41.7%			
11	SWALL: HUTH_RHIME		40.6%			
12	SWALL: Q9HU90		40.7%			
13	SWALL: HUTH_HUMAN		39.2%			
14	SWALL: HUTH_CAEEL		38.8%			
15	SWALL: Q9HLI6		41.0%			
16	SWALL: HUTH_MOUSE		38.6%			
17	SWALL: BAB29407		38.6%			
18	SWALL: HUTH_RAT		38.2%			
19	SWALL: AAG53586		39.8%			
20	SWALL: Q9KKE0		38.9%			
21	SWALL: Q9HQD5		42.2%			

[FRAELHEPLRPHPGQGRSAQNMFALADSPIVASHREGDGRVQDAYSLRCSQPVTGAARDTIAHARLVATRELAADIDNP
LAPELHA-IRPHPGQAASAAANMAAVLKSGLTGHHQDDAPRVQDAYSVRCAPQVAGAGRDTMAHAGLVAERELAAAVDNP
LAPELHA-IRPHPGQGVSAADNMSRVLAGSGLTGHQDDAPRVQDAYSVRCAPQVNGAGRDTLDHAALVAGRELASSVDNP
FQPDV-VGLRPHPGALAVAAELREFLAGSEIAPSHLTGDKVQDAYSLRAVPQVHGATWDALAQAEVLAVEFASVTDNP
FHPDIHT-LRGHKQIDAGSALRNLLQGSEIRESHIEGDERVQDPYCIRCQPVQDVGACLDLLASVARTLEIEANAVTDNP
FHPDIHT-LRGHKQIDAGSALRNLLQGSEIRESHIEGDERVQDPYCIRCQPVQDVGACLDLLASVARTLEIEANAVTDNP
FDEDIHLA-RGYQEIQIDVAERIRFYLSDSLTT--QGELRVQDAYSLRCPQVHGATWQTLGYVKEKLEIEMNAATDNP
FDPRIHR-VRGHRQTMDAATAAYRHLLVSSEIGQSHNCE-KVQDPYSLRCPQVVMGACLTQIRSAAEVLEVEANSVSDNP
FDARIHAA-RQQRGQIDVAAAYRDLLASSEVARSHKCD-KVQDPYSLRCPQVVMGACLTQMRQAAAEVLEIEANAVSDNP
FDEQIHFA-RGYVEQDVARRMESYLQDSQLTT--RQELRVQDAYSLRCPQVHGATWQTLRYVKEKLEIEMNAATDNP
FDARIHEA-RQQRGQIDTAACFRDILLGDSSEVSSHKNCD-KVQDPYSLRCPQVVMGACLTQLRQAAAEVLEIEANAVSDNP
FHPDIQHCAAIRARSTRAAA-LRQLLTGSPIRQSHIEGDERVQDPYCIRCQPVQDVGACLDLLRSVAATLTIEANAVTDNP
FDAEI-VALKPHPGMORVAANLRALLAGSQVLENAR--GIRTQDALSIIRSIPIQIHGACRDLAHARQIET-ELNSATDNP
FDTDIHA-LRPHRGQIEVAFRFRSLLSDSEIAESHRFCD-RVQDAYTLRCCPQVHGAVVNDTIAFVKNIITTELNSATDNP
YDPDIHR-IRPHRGQNLALRLRALLNPSQIAESHRNCT-KVQDAYTLRCPVQVHGAVVNDTIEFVREIITTEMNSATDNP
FTPWILGA-RPHLGQVAIGNRFRREYLTGSDIV--KRADSVKVQDAYTLRCPQVYGSVADVIDYVENVLSVEINSATDNP
FDTDIHA-VRPHRGQIEVAFRFRSLLSDSEIAESHRFCD-RVQDAYTLRCCPQVHGAVVNDTIAFVKDIITTELNSATDNP
FDTDIHA-VRPHRGQIEVAFRFRSLLSDSEIAESHRFCD-RVQDAYTLRCCPQVHGAVVNDTIAFVKDIITTELNSATDNP
FDTDIHA-VRPHRGQIEVAFRFRSLLSDSEIAESHRFCD-RVQDAYTLRCCPQVHGAVVNDTIAFVKDIITTELNSATDNP
FDARIHE-VRGQRGQIDAAALFRHVLTDTSIAIAASHNCD-KVQDPYSLRCPQVVMGACLTQMRQVAAEVLLVESNAVSDNP
AFAELPLALRQSPGLSAGEGLRDWLADSPMLAG--TAGTRTQDPLSLRAVPQVHGAAARDAFGQVAEIVDRELASVTDNP
CAPAIHE-VRPHDQAVSARHIRNLTAGSEVLDHHRDCC-RVQDAYSIIRCLPQVHGAVRDALDHLRAAVATELNSATDNP

Figure 14E

	983831	321	400
1	SWALL: CAC21618	100.0%	VVLPSGEVTSNGNFHGA
2	SWALL: HUTH_STRGR	66.1%	VVLPGDGRVESNGNFHGA
3	SWALL: HUTH_DEIRA	65.4%	VVLPGDGRVESNGNFHGA
4	SWALL: BAB16159	46.8%	LIFPTGEVSSGNGNFHGA
5	SWALL: Q9KWE4	42.0%	LVLSDNSVSSGNGNFHGA
6	SWALL: HUTH_BACSU	42.0%	LVLSDNSVSSGNGNFHGA
7	SWALL: Q9KSQ4	40.4%	LIFNDGDVSSGNGNFHGA
8	SWALL: Q9HU85	42.2%	LVFADGDISSGNGNFHGA
9	SWALL: Q9KBE6	41.7%	LVFAAGDVSSGNGNFHGA
10	SWALL: HUTH_PSEPU	39.3%	LIFDNGQVSSGNGNFHGA
11	SWALL: HUTH_RHIME	41.7%	LVFAAGDVSSGNGNFHGA
12	SWALL: Q9HU90	40.6%	LVLSDNSVSSGNGNFHGA
13	SWALL: HUTH_HUMAN	40.7%	LLLGTPEVSSGNGNFHGA
14	SWALL: HUTH_CAEEL	39.2%	MVFANGETVSSGNGNFHGA
15	SWALL: Q9HLI6	38.8%	LVFADREISSGNGNFHGA
16	SWALL: HUTH_MOUSE	41.0%	L-FNGEEVSSGNGNFHGA
17	SWALL: BAB29407	38.6%	MVFASGETISSGNGNFHGA
18	SWALL: HUTH_RAT	38.6%	MVFASGETISSGNGNFHGA
19	SWALL: AAG53586	38.2%	MVFASGETISSGNGNFHGA
20	SWALL: Q9KKE0	39.8%	LVFAANEMVSSGNGNFHGA
21	SWALL: Q9HQD5	38.9%	AVAGSPEVHSSGNGNFHGA
		42.2%	LVFPGTSSGNGNFHGA

Figure 14F

	983831	401	480
1	SWALL: CAC21618	100.0%	NKRLAVPASVDSIPSSAMQEDHVSIGWHAARKLRTSVANLRRILAVEMLIAGRALDLRAPLKPGPATGAVLEVIRSKVAG
2	SWALL: HUTH_STRGR	66.1%	LKRLAVPASADSIPSSAMQEDHVSIMGWSAARKLRTAVDNLARVIAVELYAAATRAIQREGLTTPAPASQAVVEAVRAAVEG
3	SWALL: HUTH_DEIRA	65.4%	MKRLAVPASADSIPSSAMQEDHVSIMGWSAARKLRTAVDNLARVIAVELYAAATRAIQREGLTTPAPASEAVVAALRAAGAG
4	SWALL: BAB16159	46.8%	NKVLSHPASVDSIPTSANQEDHVSIMGHAARQLRQIVANVTLSIELLCAAQGLDFQQ-LRAGRGVQAAAYEVRTFVPT
5	SWALL: Q9KWE4	42.0%	NKQMSHPASVDSIPTSANQEDHVSIMACHGARRLLAMTDNLFGILGIEALAAVQGVLELGRPLKTSPELEKAAAVALRSAPV
6	SWALL: HUTH_BACSU	42.0%	NKQMSHPASVDSIPTSANQEDHVSIMACHGARRLLAMTDNLFGILGIEALAAVQGVLELGRPLKTSPELEKAAAVALRSAPV
7	SWALL: Q9KSQ4	40.4%	NKTLAHPASVDSIPTSANQEDHVSIMGTIAARHAYQVIANTRRVIAIEAICALQAVEYRGIEHAAASYTKQLFQEMRKVVPS
8	SWALL: Q9HU85	42.2%	NKTLAHPASVDSIPTSANQEDHVSIMATFAARRLRDMGENTRGILAVEYLAQAQGLDFRAPLKSSPRIIEEARQILREKVPF
9	SWALL: Q9KBE6	41.7%	NKALAHPASVDSIPTSANQEDHVSIMAPNAGKRLWMAENVRGILAVEWLGACQGLDFREGKSSPKLEQARRLLRDKVPY
10	SWALL: HUTH_PSEPU	39.3%	NKTLAHPASVDSIPTSANQEDHVSIMGTIGSRHAYQIIQNVRNVLAIELICAMQAVDIRGREKMASFTKKILEKGREHVPY
11	SWALL: HUTH_RHIME	41.7%	NKALSHPHSVDSIPTSANQEDHVSIMAPAGKRLWMAENTRGVLAIEWLGACQGLDLRKGLKTSAKLEKARQALRSEVAH
12	SWALL: Q9HU90	40.6%	NKQLSHPASVDSIPTSANQEDHVSIMACHGARRLLQMTENLFSIIGIEALAAVQGVLELGRPLKTSPELQKAAAVALRVGSSS
13	SWALL: HUTH_HUMAN	40.7%	NRQLAQPAAVVDNFVTSALQEDHLSLGTSAALKLGRALENLRRILAEYLLAAQAFEFLLAPQRFQGTAAAWGILLRERVPA
14	SWALL: HUTH_CAEEL	39.2%	NKALCHPSSVDSIPSTSAATEDHVSIMGGWAARKALRVIEHVEQVLAIELLAACQGVLELGRPLKTTTTPLEKVDLVRSVVRP
15	SWALL: Q9HLI6	38.8%	NKVLCHPSSVDSIPTSCNQEDHVSIMGGFAARKALTVVEHVEAVLAMELLAAACQGVLELGRPLKTTTTPLEKVDLVRSVVRP
16	SWALL: HUTH_MOUSE	41.0%	NKVLAYPSSADTIPTSANQEDHVSIMGATGSLKLEIIDNVRYIIAIEYLLGSQALEFTDK-GMSPSTRKIYEKIREKVEK
17	SWALL: BAB29407	38.6%	SKALCHPSSVDSIPSTSAATEDHVSIMGGWAARKALRVVEHVEQVLAIELLAACQGVLELGRPLKTTTTPLEKVDLVRSVVRP
18	SWALL: HUTH_RAT	38.6%	SKALCHPSSVDSIPSTSAATEDHVSIMGGWAARKALRVVEHVEQVLAIELLAACQGVLELGRPLKTTTTPLEKVDLVRSVVRP
19	SWALL: AAG53586	38.2%	SKALCHPSSVDSIPSTSAATEDHVSIMGGWAARKALRVIEHVEQVLAIELLAACQGVLELGRPLKTTTTPLEKVDLVRSVVRP
20	SWALL: Q9KKE0	39.8%	NKGLCHPTSVDK-PPSANQEDHVSIMAPAGRRRLWEMAGNTRGVLAWEWLAACQGVLELGRPLKTTTTPLEKVDLVRSVVRP
21	SWALL: Q9HQD5	38.9%	NRRLAAPASLDGGITSALQEDMLTHATPAAWKALSIVDNLERILAEIILAAHRRPMSCSRKRARRRNAPLPFTGTYYARRSP
		42.2%	LRLSGQP-TLDNASVSGAQEDHVSMSAGAAYNFREAVEKAAATVVGVVELLCCGAQGREFLDPLALGAGTAAAYDLVR-EVSE

Figure 14G

	983831	481	[.	5	.] 513
1	SWALL:CAC21618	100.0%	PGQDRFLSAELEAAAYD	LLANGSVHKALEAHLPA			
2	SWALL:HUTH_STRGR	66.1%	PGPDRHLAPDLAAADA	FVRAGHLVAAAESVTGP			
3	SWALL:HUTH_DEIRA	65.4%	PGPDRFLAPDLAAADT	FVREGRLVAAVEPVTGP			
4	SWALL:BAB16159	46.8%	LTEDRYFRPDLLRLRG	ELVSGRVAQAADTQAPA			
5	SWALL:Q9KWE4	42.0%	LEDDRYMATDLKAAIE	VVASGALVSAISSGLPV			
6	SWALL:HUTH_BACSU	42.0%	LEDDRYMATDLKAAIE	VVASGALVSAISSGLPV			
7	SWALL:Q9KSQ4	40.4%	IQQDRVFSYDIERLTD	WLKKESLIPDHQNKELR			
8	SWALL:Q9HU85	42.2%	YKDRYFAPDIEKANAL	L-QLAVHNRLMPDQLL			
9	SWALL:Q9KBE6	41.7%	YQEDRFFAPDIEAASQ	LLASGCLNALLPARLLP			
10	SWALL:HUTH_PSEPU	39.3%	IDQDRMFAKDIERAAK	WLKDGSDFTKMREKER			
11	SWALL:HUTH_RHIME	41.7%	YDRDRFFAPDIEKAVE	LLAKGSLTGLLPAGLPS			
12	SWALL:Q9HU90	40.6%	IEEDRYMADDLKAAGD	LVASGRLAAAVSAGLPK			
13	SWALL:HUTH_HUMAN	40.7%	YDTRWLAPDIAASAAA	ILGERKSLARLAASIGD			
14	SWALL:HUTH_CAEEL	39.2%	WIKDRFMAPDIEAAHR	LLLEQKVWEVAAPYIEK			
15	SWALL:Q9HLI6	38.8%	PNEDRYMKPEIDAVLE	MIRENRIWEAVLPHLET			
16	SWALL:HUTH_MOUSE	41.0%	LDHDRPPSFDIETIRK	MMDKKEFISALP----			
17	SWALL:BAB29407	38.6%	WIKDRFMAPDIEAAHR	LLLDQKVWEVAAPYIEK			
18	SWALL:HUTH_RAT	38.6%	WIKDRFMAPDIEAAHR	LLLDQKVWEVAAPYIEK			
19	SWALL:AAG53586	38.2%	YDDDRFFAPDIEAAH	RLSLNKGSLVGLLPAFL--			
20	SWALL:Q9KKE0	39.8%	PIATIVR-----				
21	SWALL:Q9HQD5	38.9%	PAGDRALADDMAAVG	DLVRAGLVEDAVARALDA			
		42.2%					

Figure 14H

KEY:

983831 : HAL
1 CAC21618 : Streptomyces coelicolor
2 HUTH_STRGR : Streptomyces griseus
3 HUTH_DEIRA : Deinococcus radiodurans
4 BAB16159 : Agrobacterium rhizogenes
5 Q9KWE4 : Agrobacterium rhizogenes
6 HUTH_BACSU : Bacillus subtilis
7 Q9KSQ4 : Vibrio cholerae
8 Q9HU85 : Pseudomonas aeruginosa
9 Q9KBE6 : Bacillus halodurans
10 HUTH_PSEPU : Pseudomonas putida
11 HUTH_RHIME : Rhizobium meliloti
12 Q9HU90 : Pseudomonas aeruginosa
13 HUTH_HUMAN : Human
14 HUTH_CAEEL : Caenorhabditis elegans
15 Q9HLI6 : Thermoplasma acidophilum
16 HUTH_MOUSE : Mouse
17 BAB29407 : Mus musculus (Mouse)
18 HUTH_RAT : Rat
18 AAG53586 : uncultured bacterium pCosAS1
20 Q9KKE0 : Rhizobium meliloti
21 Q9HQD5 : Halobacterium sp

REPLACEMENT SHEET
Title: CLONING, OVEREXPRESSION AND
THERAPEUTIC USE...
Appl. No.: 09/833,745
Inventors: Joseph ROBERTS *et al.*
Attv. Docket No. 078728-0106

[illegible]

REPLACEMENT SHEET
Title: CLONING, OVEREXPRESSION AND
THERAPEUTIC USE...
Appl. No.: 09/833,745
Inventors: Joseph ROBERTS *et al.*
Atty. Docket No. 078728-0106

```

STRG 425 WSAARKLRTAVDNLARIVAVELYAATRAIELRAEGLTPAPASEAVVAALRAAGAEPPGP
HAL 427 WHAARKLRTSVANLRRILAVEMLIAGRALDLRAP--LKPGPATGAVLEVLRSKVA-GPGQ
      * * * * * * * * * * * * * * * * * * * * * * * * * * * *

```

STRG	485	DRFLAPDLAAADTFVREGRLVAAVE
HAL	484	DRFLSAELEAAYDLLANGSVHKALE